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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,555	01/27/2006	Menno Willem Jose Prins	NL030947	6159
24737	7590	02/03/2010	EXAMINER	
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			1641	
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			02/03/2010	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/566,555	PRINS, MENNO WILLEM JOSE	
	<b>Examiner</b>	<b>Art Unit</b>	
	Pensee T. Do	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 04 November 2009.
- 2a) This action is **FINAL**.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 18-24 and 26-32 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 18-24, 26-32 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ .                                    |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ .  | 6) <input type="checkbox"/> Other: _____ .                        |

**DETAILED ACTION**

***Election/Restrictions***

Applicant's election without traverse of group I, claims 18-32 in the reply filed on November 4, 2009 is acknowledged.

***Priority***

This application 10566555, PG Pub. No. 20060205093 filed 01/27/2006 is a national stage entry of PCT/IB04/51213 , International Filing Date: 07/14/2004 claims foreign priority to 03102352.6 , filed 07/30/2003.

***Amendment Entry & Claims Status***

The amendments filed on November 6, 2008 and November 4, 2009 have been acknowledged and entered.

Claims 18-24, newly added 26-32 are pending and being examined.

Claims 33-38 are canceled in the amendment filed on November 4, 2009.

***Claimed Invention***

18. (Previously Presented) A tool for distinguishing between bindings of different strengths between first and second microbiological entities, the tool comprising:

- first particles and second particles, at least one of which is magnetic,
- means for acting on the first and second particles to cause the first and second particles to exert a mechanical stress on bindings between the first and second microbiological entities to distinguish between the bindings of different strengths, the

means for acting on the first and second particles comprising at least a magnetic field generator.

### ***Withdrawn Rejections***

Rejections under 112, 2nd paragraph and 101 in the previous office action are withdrawn herein.

### ***Maintained Rejection(s)***

#### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 18-21, 22, 24, 29, 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Wilson (US 6,337,215).

Wilson teaches magnetic particles with different strengths of magnetic moments and/or different magnetic field dependencies for separating of several affinity partners simultaneously. Magnetic particles having different magnetic moments (magnetic particles with the first magnetic moment are equivalent to first particles; and magnetic particles with a second magnetic moment are equivalent to second particles of the present invention) are attached to different acceptor molecules (microbiological entity such as protein or peptide- see col. 16, lines 55-65; col. 19, lines 58-60) and a magnetic field generator (see col. 1, line 65-col. 2, line 28). When the particles are separated

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using a magnetic force, the application of such magnetic force draws the magnetic beads of same magnetic moments into a region determined by the magnetic field so that non-magnetic components can be eliminated. Beads with different magnetic moments are caused to move at different rates and thus the strengths of the particles are distinguished. Regarding claim 19, since Wilson teaches that the magnetic particles have different magnetic moments, it is inherent that the magnetic moment of one particle is greater or smaller than that of the other particle. Regarding claims 22 and 24, since the present invention describes that the magnetic field generator is a means for exerting a mechanical stress, which also includes a means for exerting a fluid frictional force and means for generating an excitation that forces a lateral movement of the particles and Wilson teaches a magnetic field generator, such magnetic field generator is capable of exerting a fluid frictional force since Wilson teaches the particles are placed in a solution (see col. 16, lines 14-25 or fig. 7) and generating an excitation that forces the particles to move laterally. Regarding claim 31, since Wilson uses the same magnetic field generator for applying a magnetic field as claimed in the present invention, such magnetic field in Wilson would have the same magnetic vector with varying direction as a function of time.

Claims 18-24, 19, 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Baselt et al. (Biosensors & Bioelectronics 13, 731-739, 1998).

Baselt teaches a biosensor that measures forces that bind DNA to DNA, antibody-antigen or ligand to receptor together. The bead array counter (BARC) use

these interaction forces to hold magnetic microbeads to a solid substrate.

Microfabricated magnetoresistive transducers on the substrate indicate whether or not the beads are removed when pulled by magnetic forces. By adapting magnetoresistive computer memory technology, it is possible to fabricate millions of transducers on a chip and detect or screen thousands of analytes. (see abstract). Since Baselt teaches that multi-analytes are detected or screened, there must be more than one types of magnetic particles, one type for each different analyte. Baselt teaches that the target molecule bridges the substrate and a magnetic microbead. (see pg 733, magnetic bead assays). Regarding claim 19, since Baselt teaches that the magnetic particles have different magnetic moments, it is inherent that the magnetic moment of one particle is greater or smaller than that of the other particle. Thus, the magnetic beads are attached to the target molecule which is an antigen (protein) or DNA. Regarding claim 24, since the specification fails to describe any structure of the means for generating an excitation that forces a lateral movement of the particles with respect to the array, the magnetic field generator in Baselt is equivalent to such means because the magnetic field generator can be placed on any side of the substrate/array to attract the magnetic particles to move laterally towards the magnetic field. Regarding claims 22 and 24, since the present invention describes that the magnetic field generator is a means for exerting a mechanical stress, which also includes a means for exerting a fluid frictional force and means for generating an excitation that forces a lateral movement of the particles and Baselt teaches a magnetic field generator, such magnetic field generator is capable of exerting a fluid frictional force and generating an excitation that forces the

particles to move laterally. Regarding claim 31, since Baselt uses the same magnetic field generator for applying a magnetic field as claimed in the present invention, such magnetic field in Baselt would have the same magnetic vector with varying direction as a function of time.

### ***New Grounds of Rejection***

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 26 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wilson or Baselt in view of Summerton (US 6,060,246) .

Wilson and Baselt have been discussed above.

However, they fail to teach that the second magnetic particle is not bound to any microbiological entities.

Summerton teaches “Capture of .alpha.-Globin RNA. As an illustration of the method, capture particles were prepared by binding morpholino oligomers to the surface of [REDACTED] beads (M-280), as described in Example 3. A [REDACTED] contained a U.sub.25 probe (a 25-mer poly-uracil morpholino oligomer, SEQ ID NO: 1) bound via a PEG spacer group and a disulfide linker group. A [REDACTED] [REDACTED] contained a probe, designated Neu-Probe.TM. 124, complementary to an .alpha.-globin RNA transcript (SEQ ID NO: 2). A third particle, constituting

the rapid pairing reagent, contained both probes. ***Also included were M-280 beads having no attached probes, as a control for nonspecific sticking to the particles***". (see col. 12, lines 45-57).

It would have been obvious to one of ordinary skills in the art to use a magnetic bead having no attached probes as taught by Summerton for use as a control for nonspecific sticking to the particles as a control particle in the method of Wilson or Baselt since these references all teaches using multiple different magnetic particles for separating different analytes in a sample.

Claims 27, 30 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wilson or Baselt in view of Mirkin (US 6,984,491).

Wilson and Baselt have been discussed above.

However, they fail to teach a capture reagent for capturing both first target-first particle complex and second target-second particle complex; and that the second microbiological entities include capture molecules while the first microbiological entities are target molecules.

Mirkin teaches a first particle coupled to a capture molecule and a second particle coupled to a target molecule. The capture molecule and the target molecule hybridize. (see figure 1). Mirkin also teaches that the first particle and the second particles can be magnetic. (see col. 37, lines 44-47). Mirkin also teaches that the first particle coupled to a first nucleic acid sequence hybridizes to a part of a capture

molecule and a second particle coupled to a second nucleic acid sequence hybridizes to a second part of the capture molecule. (see fig. 3).

Since it is well known in the art as taught by Mirkin that different assay configurations can be applied using two magnetic particles, it would have been obvious to one of ordinary skills in the art to incorporate the concept of different assay configurations as taught by Mirkin in the method of Wilson or Baselt so that nucleic acids can be manipulated using different magnetic particles.

***Response to Arguments***

Applicant's arguments filed November 6, 2009 have been fully considered but they are not persuasive.

Regarding the 102 rejections by Wilson and Baselt, Applicants argue that Wilson and Baselt fail to teach any means for acting on first and second particles to cause the first and second particles to exert a mechanical stress on bindings between the first and second microbiological entities to distinguish between the bindings of different strengths. Applicants further submit that Baselt does not disclose first and second particles.

The present claims recite that the means [for acting on first and second particles to cause the first and second particles to exert a mechanical stress on bindings between the first and second microbiological entities to distinguish between the bindings of different strengths] is a magnetic field generator. Wilson and Baselt both disclose using

magnetic field generators. Thus, the magnetic field generators in Wilson and Baselt should be able to perform the same functions as claimed in the present invention.

Regarding the issue that Baselt does not disclose first and second particles, Baselt teaches that magnetic particles are used to screen thousands of different analytes, thus there must be more than one types of magnetic particles. Each type of particles has an affinity ligand specific for one type of analyte.

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Pensee T. Do/  
Examiner, Art Unit 1641

/Mark L. Shibuya/  
Supervisory Patent Examiner, Art Unit 1641